Necrotizing Fasciitis from *Pseudomonas aeruginosa* in Infantile Acute Lymphoblastic Leukaemia

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Sir,

Necrotizing fasciitis (NF) is a rare, rapidly progressive and life-threatening infection of the subcutaneous tissue and the superficial fascia. In the past this clinical entity was known as necrotizing erysipelas, haemolytic streptococcus gangrene, suppurative fasciitis or hospital gangrene (1, 2). In 1924, Meleney (3) reported a large number of such cases with tissue cultures positive for haemolytic streptococcus. In 1952, Wilson (4) used the term NF for the first time and observed that no specific micro-organism was involved in the pathogenesis of this infection. A polybacterial cause of NF is frequent and at present well documented (1, 5). We report a case of NF in a boy affected by acute lymphoblastic leukaemia (ALL) in which *Pseudomonas aeruginosa* was the only isolate from the affected skin and subcutaneous tissue, urine, faeces and blood.

CASE REPORT

A 7-month-old boy was hospitalized for an early Pre-B HLA-DR+, CD19+, CD10- ALL. The patient was assigned to the high-risk group and induction therapy in accordance with the AIEOP (Italian Association of Pediatric Hematologic Oncology) ALL–9503 protocol was performed. At day 25 of induction therapy (methotrexate, daunomycin, cytosine-arabinoside, vincristine, L-asparaginase and prednisone) he presented fever (38.4°C). Laboratory testing revealed bone marrow aplasia (leucocyte count 0.6×10^9/l; neutrophils 4%; lymphocytes 94%; haemoglobin 1.43 mmol/l; platelet count 6×10^9/l) and increased C-reactive protein (22.6 mg/dl). His perianal region showed an erythematous and oedematous area, with anal erosions and ecchymoses. Soft tissue ultrasonography revealed minimal subcutaneous oedema. Parenteral antibiotic therapy with amikacin and ceftazidine was initiated. Despite antimicrobial drug therapy, the boy was febrile and his general condition rapidly worsened. The following day the lesion extended to his lower abdomen, pubis, perineum and buttocks and both the anal erosion and the ecchymotic area had widened. A sharp margin delineated the affected area (Fig. 1A). Teicoplanin and metronidazole were added to the therapy and concentrated red blood cells and platelets were transfused. High doses of intravenous immune globulin and granulocyte colony-stimulating factor (G-CSF) were also included. However, the clinical aspect rapidly worsened in a few hours. A purple ecchymotic plaque with eroded necrotic areas developed extending to the buttocks and the intergluteal folds. A deep spontaneous fistula draining purulent exudate also appeared (Fig. 1B).

Skin, blood, urine and faeces cultures were all positive for *P. aeruginosa*. The successive sonographic study of the lesion showed a marked and diffuse thickening of the perineal and perianal subcutaneous tissue with evidence of a subscrotal hypoechogenous area. The fascia, partially visible, was thickened.

Surgical debridement of all the devitalized tissues was carried out. A biopsy specimen showed necrosis of the cutis and the subcutaneous tissue with presence of bacteria. A temporary colostomy was performed and two minor debridements of the wound were carried out. Antibiotic therapy was continued for 3 weeks. The

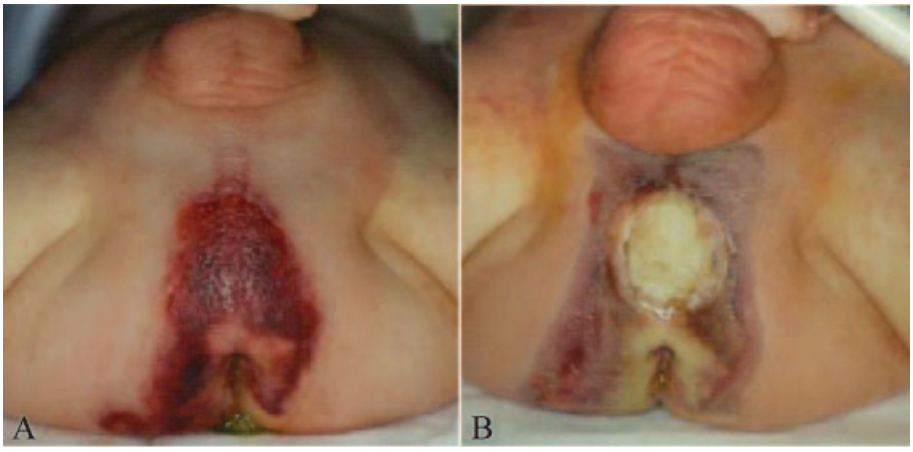

Fig. 1. (A) A large oedematous and erythematous lesion with wide perianal erosion and ecchymotic area. (B) An ecchymotic plaque with necrotic areas extending to the buttocks and intergluteal folds – this photo was taken a few hours after (A).

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patient also underwent hyperbaric oxygen treatment (30 sessions), which resulted in a progressive improvement of the anal lesions.

During the following 2 years, the boy developed an anal stenosis. He underwent reconstructive plastic surgery and anal dilatation. The colostomy was maintained up to 4 years of age. At present the patient is 6 years old and is under surgical follow-up with an acceptable level of anal functionality.

DISCUSSION

NF is rare in childhood, with an incidence of 0.08 per 100 000/year (6). Its association with ALL has been described in only a few cases (1, 7–10). The paediatric cases reported (1, 5, 10) are frequently caused by group A beta-haemolytic streptococci (GABHS), but also by many other aerobic and anaerobic bacteria (such as *P. aeruginosa*, *Peptostreptococcus* spp., *Bacteroides fragilis* group, *Staphylococcus aureus*, *Enterobacter cloacae*, *Klebsiella pneumoniae*) and, in rare cases, by fungi. NF has been reported as being polymicrobial in 71–75% of cases (1, 5).

In a series of 39 paediatric cases of NF, *P. aeruginosa* was isolated in 7 patients, but always in association with other germs (*E. cloacae*, *K. pneumoniae*, *Strep. faecium*, *Escherichia coli*, *Staph. aureus*, GABHS) (1). In our patient only *P. aeruginosa* was isolated from the blood, urine, faeces and skin cultures. *P. aeruginosa* is rarely reported as the only causative agent of this condition in children (9, 10).

Paediatric NF due to *P. aeruginosa* may present malnutrition, spondylitis, juvenile rheumatoid arthritis and ALL as underlying factors (1, 9, 10) and varicella, trauma, surgery and chemotherapy, especially for ALL, as initiating factors (1, 5). In children NF may affect the trunk, the lower extremities and the genital area. The predisposing factors for this localization are diabetes, surgical genital procedures, rectal perforation and immunosuppression (1).

NF is often misdiagnosed as erysipelas or cellulitis. Like cellulitis, NF presents initially with oedema and erythema, but the oedema in NF is generally harder. Tissue crepitation is a suggestive but rare sign of NF (11). Furthermore, in the presence of unresponsiveness to antibiotic treatment in 24–48 h, NF should be suspected (1). The clinical diagnosis can be supported by ultrasonography, which shows a distorted and thickened fascia, turbid fluid or loculate abscess in the fascial plane, subcutaneous tissue swelling with normal muscle plane (10), as in our patient.

Early treatment with clindamycin and cefoperazone sodium is recommended (1), while amikacin and ceftazidime have been employed in the presence of *P. aeruginosa* (10). However, antibacterial therapy must be adjusted according to culture findings (1). Antibiotics alone are not able to reach necrotic tissue and have poor effectiveness, if surgical debridement is not performed early to reduce the progression of tissue necrosis (1). The average mortality ranges from 10% to 60% in children (12) and it doubles when surgery is delayed for more than 24 h (1). Hyperbaric oxygen exerts direct toxicity on anaerobes, increases tissue oxygen pressure, improves neutrophil granulocytes bactericidal activity and increases antibiotic activity; however, double-blind randomized studies are lacking (13, 14).

As granulocytopenia predisposes to infections from *P. aeruginosa*, G-CSF contributed to a favourable outcome in one case (10). In our patient early surgical and antimicrobial treatment with hyperbaric oxygen therapy contributed to the favourable outcome, while G-CSF did not influence the course of the infection.

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